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10/735,442	12/12/2003	Qiong Cheng	CL2027 US NA	2513

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EXAMINER	
FRONDA, CHRISTIAN L	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 04/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,442	CHENG ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-27 is/are pending in the application.

4a) Of the above claim(s) 17-27 is/are withdrawn from consideration.

5)☒ Claim(s) 16 is/are allowed.

6)☒ Claim(s) 1-5 is/are rejected.

7)☒ Claim(s) 6-15 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 12 December 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 03/04;09/04;02/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-16, drawn to a bacteria that overproduces a carotenoid, classified in class 435, subclass 252.3.

II. Claims 17-27, drawn to a method for the production of a carotenoid, classified in class 435, subclass 67.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I and Group II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product such as using the bacteria of Group I in a recombinant process for producing a polypeptide.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and classification, restriction for examination purposes as indicated is proper.

3. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.
In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined.

See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

4. During a telephone conversation with S. Neil Feltham on 02/09/2006, a provisional election was made without traverse to prosecute the invention of Group I, claims 1-16. Affirmation of this election must be made by applicant in replying to this Office action. Claims 17-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

6. Claims 1-16 are under consideration in this Office Action.

7. In the **DECLARTION OF BIOLOGICAL CULTURE DEPOSIT** filed 12/12/03, applicants have stated that all restrictions on the availability to the public of bacterial strains ATCC PTA-4807 and ATCC PTA-4823 will be removed upon granting of a U.S. patent on the instant application. Accordingly, applicants' declaration and statement regarding the availability of the said bacterial strains ATCC PTA-4807 and ATCC PTA-4823 meet the enablement requirement for claim 16.

8. Claims 6-15 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. Furthermore, claim 8 is in improper form because a multiple dependent claim should refer to other claims in the

alternative only. See MPEP § 608.01(n).

Accordingly, claims 6-15 have not been further treated on the merits.

Claim Rejections - 35 U.S.C. § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 1-5 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

The claims, as written, does not sufficiently distinguish over carotenoid producing bacteria as they exist naturally because the claim does not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). See MPEP 2105.

The claims should be amended to indicate the hand of the inventor, e.g., by insertion of the phrase "An isolated carotenoid overproducing bacteria".

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 3, line 3, the phrase "*ispB lytB* and *dxr yjeR*" renders the claim vague and indefinite. The metes and bounds of the claim are unclear since it is not certain what is meant by this phrase, which occurs after the end of the sentence of claim 3

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the evaluation of the claims for compliance with the written description requirement of 35 U.S.C. 112, of particular relevance is 66 FR 1099, Friday, January 5, 2001,which states:

> "*Eli Lilly* explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of compounds is claimed. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406. Thus *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed." (see p. 1100, 1st column, line 47 to 2nd column, line 2).

The claims are genus claims which are drawn to a genus of carotenoid overproducing bacteria comprising a genus of genes encoding a functional carotenoid enzymatic biosynthetic pathway wherein any dxs, idi, and ygbBP genes of any nucleotide sequence and structure are overexpressed and wherein any yjeR gene of any nucleotide sequence and structure is down regulated. The scope of the genus of carotenoid overproducing bacteria includes many members with widely differing biochemical and biophysical properties. The scope of the genus of genus of genes encoding a functional carotenoid enzymatic biosynthetic pathway includes many members with widely differing structural, chemical, and physiochemical properties including widely differing nucleotide or amino acid sequences. Furthermore, each genus is highly variable because a significant number of structural differences between genus members exist.

The specification discloses two *E.coli* carotenoid overproducing strains identified as ATCC PTA-4807 and ATCC PTA-4823. The specification discloses the following genes from *Pantoea stewartii* and their respective nucleotide SEQ ID NO identifiers: CrtE (SEQ ID NO: 1), CrtX (SEQ ID NO: 3), CrtY (SEQ ID NO: 5), CrtI (SEQ ID NO: 7), CrtB (SEQ ID NO: 9), and CrtZ (SEQ ID NO: 11) [see p. 5]. The specification discloses the following genes from *Methylomonas*16a and their respective nucleotide SEQ ID NO identifiers: dxs (SEQ ID NO: 13), lytB (SEQ ID NO: 15), and dxr (SEQ ID NO: 17) [see p. 6]. The specification discloses that SEQ ID NO: 63 is the nucleotide sequence of a mutant yjeR gene, which is identified as yjeR::Tn5.

However, the specification does not describe and define any properties, such as structural features and nucleotide or amino acid sequences, which are commonly possessed by members of each claimed genus. For example, the specification does not does not describe and define any structural features and nucleotide or amino acid sequences commonly possessed by yjeR genes from biological sources other than the disclosed mutant yjeR gene of SEQ ID NO: 63. Furthermore, the specification does not describe and define any properties commonly shared between members of the claimed genus of carotenoid overproducing bacteria. The specification does not provide additional species within this genus, other than ATCC PTA-4807 and ATCC PTA-4823, which are representative of the claimed genus of carotenoid overproducing bacteria. Thus, one skilled in the art cannot predict and visualize or recognize the identity of the members of each genus for use in the claimed method.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v, Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of a genus of carotenoid overproducing bacteria comprising a genus of genes encoding a functional carotenoid enzymatic biosynthetic pathway wherein any dxs, idi, and ygbBP genes of any nucleotide sequence and structure are overexpressed and wherein any yjeR gene of any nucleotide sequence and structure is down regulated.

The claims are additionally rejected for the following reasons. The claims encompass the genes dxs, dxr, ygpP, ychB, ygbB, lytB, idi, ispA, ispB, crtE, crtB, crtI, crtY, crtZ, crtW, and yjeR. Gene elements which are not particularly described, including promoter regions, regulatory elements, and untranslated regions, are essential to the function of the claimed invention since the claims recite "gene". The art indicates that the structure of these gene elements are empirically determined. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art.

There is no known or disclosed correlation between the coding region of a polynucleotide encoding a protein or enzyme and the structure of the non-described promoter regions, regulatory elements, and untranslated regions. In view of the above considerations, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of any dxs, dxr, ygpP, ychB, ygbB, lytB, idi, ispA, ispB, crtE, crtB, crtI, crtY, crtZ, crtW, and yjeR gene.

15. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated *E.coli* host cell transformed with a polynucleotide comprising SEQ ID NO: 63 which encodes a mutant oligoribonuclease, where said isolated *E.coli* cell comprises a functional carotenoid enzymatic biosynthetic pathway consisting of the proteins of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, and 18; does not reasonably provide enablement for any other embodiment as recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any carotenoid overproducing bacteria comprising any genes encoding a functional carotenoid enzymatic biosynthetic pathway wherein any dxs, idi, and ygbBP genes of any nucleotide sequence and structure are overexpressed and wherein any yjeR gene of any nucleotide sequence and structure is down regulated.

The specification provides guidance and working examples for two *E.coli* carotenoid overproducing strains identified as ATCC PTA-4807 and ATCC PTA-4823. The specification guidance and working examples for the following genes from *Pantoea stewartii* and their respective nucleotide SEQ ID NO identifiers: CrtE (SEQ ID NO: 1), CrtX (SEQ ID NO: 3),

CrtY (SEQ ID NO: 5), CrtI (SEQ ID NO: 7), CrtB (SEQ ID NO: 9), and CrtZ (SEQ ID NO: 11) [see p. 5]. The specification provides guidance and working examples for the following genes from *Methylomonas*16a and their respective nucleotide SEQ ID NO identifiers: dxs (SEQ ID NO: 13), lytB (SEQ ID NO: 15), and dxr (SEQ ID NO: 17) [see p. 6]. The specification provides guidance and working examples for SEQ ID NO: 63, which is the nucleotide sequence of a mutant yjeR gene that is identified as yjeR::Tn5.

However, the specification does not provide guidance, prediction, and working examples for any other carotenoid overproducing bacteria comprising any genes encoding a functional carotenoid enzymatic biosynthetic pathway wherein any dxs, idi, and ygbBP genes of any nucleotide sequence and structure are overexpressed and wherein any yjeR gene of any nucleotide sequence and structure is down regulated. The specification does not provide guidance, prediction, and working examples for any of the genes dxs, dxr, ygpP, ychB, ygbB, lytB, idi, ispA, ispB, crtE, crtB, crtI, crtY, crtZ, crtW, and yjeR from any biological source and nucleotide sequence and structure.

Thus, an undue amount of trial and error experimentation must be preformed where such experimentation involves searching and screening a vast number of biological sources for any carotenoid overproducing bacteria comprising any genes encoding a functional carotenoid enzymatic biosynthetic pathway, wherein any dxs, idi, and ygbBP genes of any nucleotide sequence and structure are overexpressed and wherein any yjeR gene of any nucleotide sequence and structure is down regulated. Alternatively, trial and error experimentation involves searching and screening for the genes dxs, dxr, ygpP, ychB, ygbB, lytB, idi, ispA, ispB, crtE, crtB, crtI, crtY, crtZ, crtW, and yjeR from any biological source; transforming these genes into any bacteria; overexpressing the dxs, idi, and ygbBP genes and mutating the yjeR gene such that it is down regulated in the bacteria; and then determining whether the bacteria can overproduce any carotenoid. General teachings from the specification regarding screening and searching for the claimed invention is not guidance for making the claimed invention.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific SEQ ID NO of each of the genes coding for the enzymes involved in carotenoid biosynthesis and the specific SEQ ID NO of the yjeR gene that is down regulated. Without such a guidance, the amount of experimentation left to those skilled in the art to make the invention is undue and well outside of routine experimentation.

Conclusion

16. Claim 16 is allowed.

17. The following reference made of record and not relied upon is considered pertinent to applicant's disclosure: Zhang et al. (J Bacteriol. 1998 May;180(10):2779-81) teach the *E.coli* oligoribonuclease enzyme encoded by the yjeR (o204a) gene.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

19. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

TEKCHAND SAIDHA
PRIMARY EXAMINER